

What is claimed is:

1. A method of non-enzymatic ligation of a nucleic acid, comprising contacting a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide under 5 conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide.

2. The method of claim 1, wherein said polynucleotide-3' phosphorothiolate further comprises a 3' 10 SNP moiety.

3. The method of claim 1, wherein said polynucleotide-3' phosphorothiolate further comprises a duplex polynucleotide.

4. The method of claim 1, wherein said acceptor 15 polynucleotide further comprises a duplex polynucleotide.

5. The method of claim 1, further comprising transducing into a host cell a polynucleotide-3' phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide.

6. The method of claim 1, further comprising the step:

contacting a polynucleotide-3'
phosphorothiolate precursor and an activator under
5 conditions sufficient to react said polynucleotide-3'
phosphorothiolate precursor and said activator to produce
said polynucleotide-3' phosphorothiolate.

7. The method of claim 6, wherein said activator
10 is iodonitrobenzene.

8. A method of molecular cloning comprising,
contacting an insert comprising a polynucleotide-3'
phosphorothiolate with an acceptor vector under conditions
that allow formation of a phosphodiester bond between said
15 insert and said acceptor vector to generate a vector
comprising an insert polynucleotide.

9. The method of claim 8, further comprising
transforming said vector comprising an insert polynucleotide
into a host cell.

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10. The method of claim 8, wherein said
polynucleotide-3' phosphorothiolate further comprises a 3'
SNP moiety.

11. The method of claim 8, further comprising the
25 step:

contacting a polynucleotide-3'
phosphorothiolate precursor and iodonitrobenzene under
conditions sufficient to react said polynucleotide-3'

phosphorothiolate precursor and said iodonitrobenzene to produce said polynucleotide-3' phosphorothiolate.

12. A method of molecular cloning comprising,
5 contacting a vector comprising a polynucleotide-3'
phosphorothiolate with an acceptor polynucleotide, under
conditions that allow formation of a phosphodiester bond
between said vector and said acceptor polynucleotide to
generate a vector comprising said acceptor polynucleotide.

10 13. The method of claim 12, further comprising
transforming said vector comprising said acceptor
polynucleotide into a host cell.

14. The method of claim 12, wherein said
15 polynucleotide-3' phosphorothiolate further comprises a 3'
SNP moiety.

15. The method of claim 12, wherein said vector
further comprises a 3' phosphorothiolate moiety at one or
more terminal ends.

20 16. The method of claim 12, further comprising
the step:
contacting a polynucleotide-3'

phosphorothiolate precursor and an activator under
25 conditions sufficient to react said polynucleotide-3'
phosphorothiolate precursor and said activator to produce
said polynucleotide-3' phosphorothiolate.

17. A kit, comprising:

- (a) a polynucleotide-3'
phosphorothiolate; and
- (b) a buffer in an aqueous solution.

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18. The kit of claim 17, wherein said
polynucleotide-3' phosphorothiolate further comprises one or
more 3' phosphorothiolate moieties.

10 19. The kit of claim 17, wherein said
polynucleotide-3' phosphorothiolate further comprises a
single stranded polynucleotide.

15 20. The kit of claim 18, wherein said single
stranded polynucleotide further comprises an
oligonucleotide.

21. The kit of claim 17, wherein said
polynucleotide-3' phosphorothiolate further comprises a
duplex polynucleotide.

20 22. The kit of claim 17, wherein said
polynucleotide-3' phosphorothiolate comprises a 3'-SNP
moiety.

23. A kit, comprising:

- 25 (a) a polynucleotide-3'
phosphorothiolate precursor; and
- (b) an activator.

24. The kit of claim 23, wherein said polynucleotide-3' phosphorothiolate further comprises one or more 3' phosphorothiolate moieties.

5 25. The kit of claim 24, wherein said polynucleotide-3' phosphorothiolate further comprises a single stranded polynucleotide.

26. The kit of claim 24, wherein said single stranded polynucleotide further comprises an 10 oligonucleotide.

27. The kit of claim 24, wherein said polynucleotide-3' phosphorothiolate further comprises a duplex polynucleotide.

15 28. The kit of claim 24, wherein said polynucleotide-3' phosphorothiolate comprises a 3'-SNP moiety.

29. A method of ligating a nucleic acid, comprising contacting a polynucleotide-5' phosphorothiolate 20 with a non-sequence specific topoisomerase, or a fragment or modification thereof, and an acceptor polynucleotide under conditions that allow formation of a phosphodiester bond between said polynucleotide-5' phosphorothiolate and said acceptor polynucleotide, with the proviso that said 25 polynucleotide-5' phosphorothiolate does not contain the nucleotide sequence G(C/T)CCTT (SEQ ID NO:5).

30. The method of claim 29, wherein said topoisomerase is human topoisomerase I, or a fragment or modification thereof.

31. The method of claim 30, wherein said human topoisomerase I is Topo65, or a fragment or modification thereof.

32. The method of claim 29, wherein said polynucleotide-5' phosphorothiolate further comprises a duplex polynucleotide.

10 33. The method of claim 29, wherein said acceptor polynucleotide further comprises a vector.

34. The method of claim 29, wherein said polynucleotide-5' phosphorothiolate further comprises a vector.

15 35. The method of claim 29, wherein said polynucleotide-5' phosphorothiolate further comprises a polynucleotide having a 5' phosphorothiolate moiety incorporated within four base pairs from a 3' end of said polynucleotide-5' phosphorothiolate.

36. A kit, comprising:

(a) a polynucleotide-5'
phosphorothiolate, with the proviso that said
polynucleotide-5' phosphorothiolate does not contain a
5 nucleotide sequence selected from the group of
SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7;
(b) a non-sequence specific
topoisomerase, or fragment or modification thereof having
topoisomerase activity.

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37. The kit of claim 36, wherein said
topoisomerase is human topoisomerase I, or a fragment or
modification thereof.

38. The kit of claim 37, wherein said
15 topoisomerase is Topo65, or a fragment or modification
thereof.

39. The kit of claim 36, wherein said
polynucleotide-5' phosphorothiolate is a single stranded
polynucleotide-5' phosphorothiolate.

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40. The kit of claim 37, wherein said single
stranded polynucleotide-5' phosphorothiolate further
comprises an oligonucleotide.

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41. The kit of claim 36, wherein said
polynucleotide-5' phosphorothiolate further comprises a
duplex polynucleotide-5' phosphorothiolate.

42. The kit of claim 41, wherein said duplex polynucleotide-5' phosphorothiolate further comprises one or more terminal end overhangs.

43. The kit of claim 42, wherein said one or more 5 terminal end overhangs further comprise a nucleotide sequence complementary to one or more restriction endonuclease cleavage sites.

44. A composition comprising,
10 (a) a polynucleotide-5'
phosphorothiolate, with the proviso that said
polynucleotide-5' phosphorothiolate does not contain a
nucleotide sequence selected from the group of SEQ ID NO:5,
SEQ ID NO:6 or SEQ ID NO:7; and
15 (b) a non-sequence specific
topoisomerase, or fragment or modification thereof having
topoisomerase activity.

45. The composition of claim 44, wherein said
20 topoisomerase is human topoisomerase I, or a fragment or
modification thereof.

46. The composition of claim 45, wherein said
topoisomerase is Topo65, or a fragment or modification
thereof.

25 47. The composition of claim 44, wherein said
polynucleotide-5' phosphorothiolate is a single stranded
polynucleotide-5' phosphorothiolate.

48. The composition of claim 47, wherein said single stranded polynucleotide-5' phosphorothiolate further comprises an oligonucleotide.

49. The composition of claim 44, wherein said 5 polynucleotide-5' phosphorothiolate further comprises a duplex polynucleotide-5' phosphorothiolate.

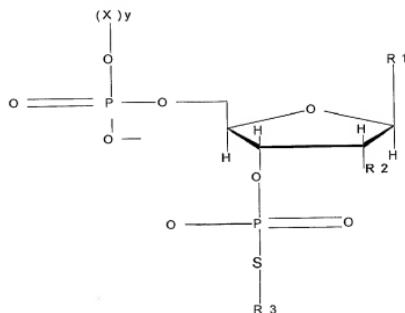
50. The composition of claim 49, wherein said duplex polynucleotide-5' phosphorothiolate further comprises 10 one or more terminal end overhangs.

51. The composition of claim 50, wherein said one or more terminal end overhangs further comprise a nucleotide sequence complementary to one or more restriction endonuclease cleavage sites.

52. A compound of the formula:

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wherein,

X is a nucleotide;

y is a positive integer;

R1 is a nucleotide base;

R2 is H or OH; and

R3 is a halo, alkyl, substituted alkyl,
sulfonate moiety, phenyl,
substituted phenyl.

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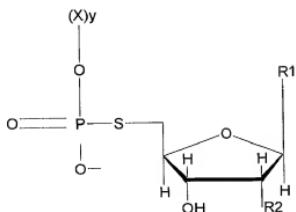
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53. The compound of claim 52, wherein
R2 is H.

54. The compound of claim 52, wherein
R3 is nitrophenyl.

25 55. The compound of claim 52, further comprising
a complementary polynucleotide.

56. A compound of the formula:



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wherein,
X is a nucleotide;
y is a positive integer;
R1 is cytosine or guanine; and
R2 is H or OH.